Pharmoptima®

A GENESIS DRUG DISCOVERY & DEVELOPMENT COMPANY

OVERVIEW OF SERVICES

GD3 Genesis
Drug Discovery & Development

Chemistry
- Venenum Biodesign Chemistry
- NEDP New England Discovery Partners
- BioBlocks
- Organochem — Accelerate Your Business

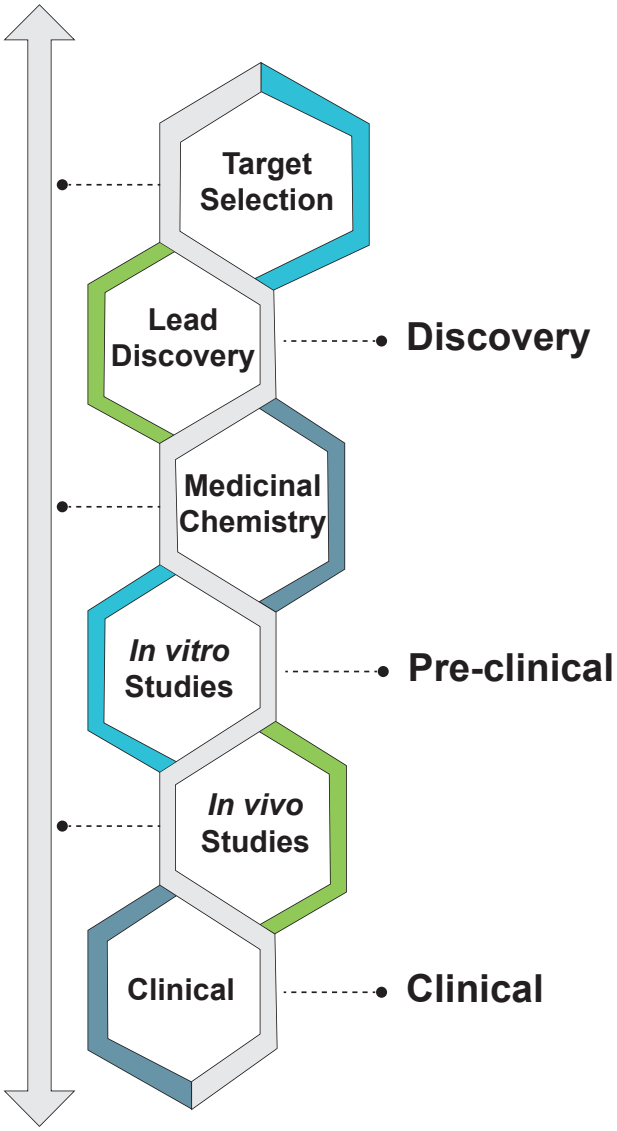
Biology/ Bioanalytical
- ias integrated analytical SOLUTIONS
- Venenum Biodesign Biology
- Pharmoptima
- Ingenio Diagnostics

Disease Modeling
- Invivotek
- nexus pharma

Preclinical-Toxicology
- Comparative Biosciences Inc.

Clinical
- STATKING Clinical Services
- JSS RESPONSIVE RELIABLE RESULTS

Genesis Drug Discovery & Development (GD³) is is a fully integrated CRO providing services to support drug discovery programs of our clients from target discovery through IND filing and managing Phase I-IV clinical trials. GD³ portfolio includes services for HTS and assay development, synthetic organic and medicinal chemistry, DMPK/in-vivo pharmacology and safety pharmacology, toxicology as well as clinical trial services for the regulatory approval of novel drug and medical device products.



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PharmOptima

Since 2003, PharmOptima has been advancing drug discovery by providing *in vitro* and *in vivo* contract research services

Founded by scientists with broad expertise and years of pharmaceutical experience, Pharmoptima truly understands the value of solving the complex problems associated with drug development. Since 2003, PharmOptima has been advancing drug discovery and development in various therapeutic areas and has filled a niche in ocular drug development.

PharmOptima's proven approach to drug discovery and optimization focuses on our ability to maximize your program's success by developing customized solutions for your intellectual property problems and providing the highest quality data in a rapid timeframe to move your compound up the value chain. Our multidisciplinary scientific team consults with you to provide research strategies to optimize your success.

Services

PharmOptima is a leading contract research organization (CRO) specializing in preclinical research in various therapeutic areas including ocular research. Our portfolio of services provides powerful tools and valuable solutions to develop your compounds and advance your therapeutic candidates.

We provide expertise in:

- Drug Metabolism & Pharmacokinetic Studies
- Ocular Services
- Bioanalytical
- Ligand Binding & Other Assays
- Molecular Biology and Biochemistry
- Bioanalytical
- *In Vivo* Techniques

Drug Metabolism & Pharmacokinetic Studies

We are experienced at conducting *in vivo* pharmacokinetic and drug metabolism studies absorption, distribution, metabolism, and excretion (ADME). Our *in vivo* proof of concept testing and model development is designed to confirm drug delivery, efficacy, and tolerance in rodents and rabbits

Services:

- Pharmacokinetic analysis of blood (plasma)
- Metabolite isolation and characterization
- Bioequivalence studies
- Formulation screening and optimization
- Bioavailability studies including oral (PO), subcutaneous (SC), intramuscular (IM), Intraperitoneal (IP), and Intratracheal
- Single dose and multiple dose PK studies
- Discovery liquid formulation development and optimization
- Drug distribution in tissue/organ and body fluid and determination of blood and brain ratio for brain penetration
- Metabolic kinetics with active metabolites
- PK study for design of dose and dose regimen in various rodent disease models
- PK analysis using WinNonlin®

Ocular Services

Our ophthalmic services are accompanied by a high level of technical expertise.

From specialized ocular dosing by trained scientists, to the precise dissection of specific ocular tissues by our specialists, followed by exacting sample processing and bioanalysis by PharmOptima's experienced staff; we stand out against the large CRO model of generalized necropsy technicians and crash & shoot discovery bioanalysis. Our bioanalytical team has extensive experience processing, homogenizing and extracting ocular fluids and tissues. We have developed LC-MS/MS methods for hundreds of compounds.

With over 40 years of combined experience, PharmOptima and its sister company Comparative Biosciences have teamed up to provide a comprehensive portfolio of ocular drug discovery, development, safety, and pharmacokinetic services. A team of industry-trained scientists and veterinary ophthalmologist collaboration to ensure the efficient development and coordination of your unique preclinical ocular program, from target validation and assay development to identification and optimization of clinical candidates.

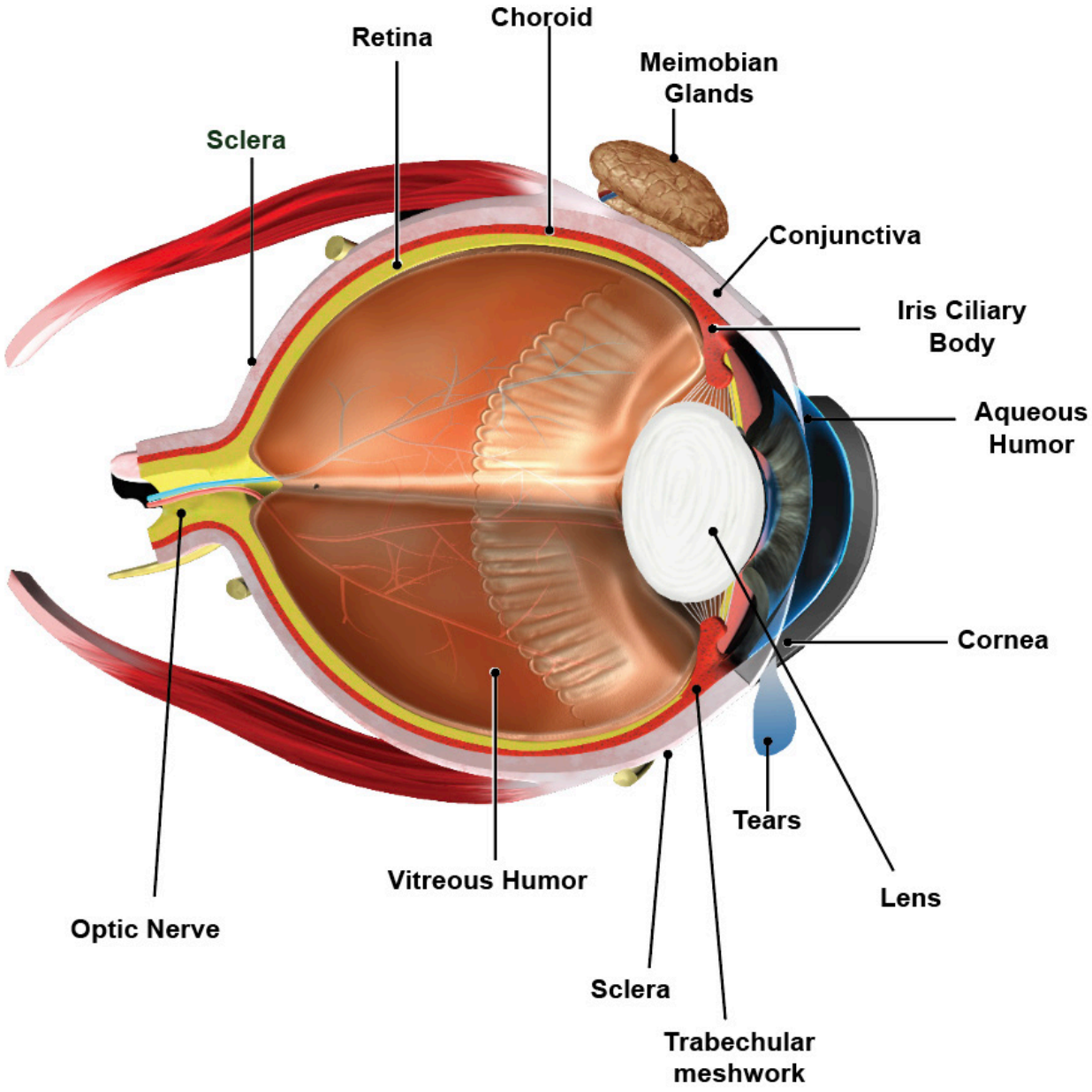
Services:

- validate bioanalytical methods following current FDA Crystal City and OECD guidances
- perform cross validations for additional species and matrices
- assay plasma and dosing solutions from regulated animal safety studies (i.e. GLP) and clinical trials
- assay metabolism of drugs/prodrugs in ocular tissue

Ocular Matrices Collected for PK:

- Conjunctiva
  - o Palpebral
  - o Bulbar
- Cornea
- Aqueous Humor
- Iris-ciliary Body
- Meibomian Gland
- Lacrimal Gland
- Vitreous Humor
- Retina
- Choroid
- Sclera
- Optic Nerve
- Lens
- Trabecular Meshwork
- Tears

Ocular Matrices Collected for PK:



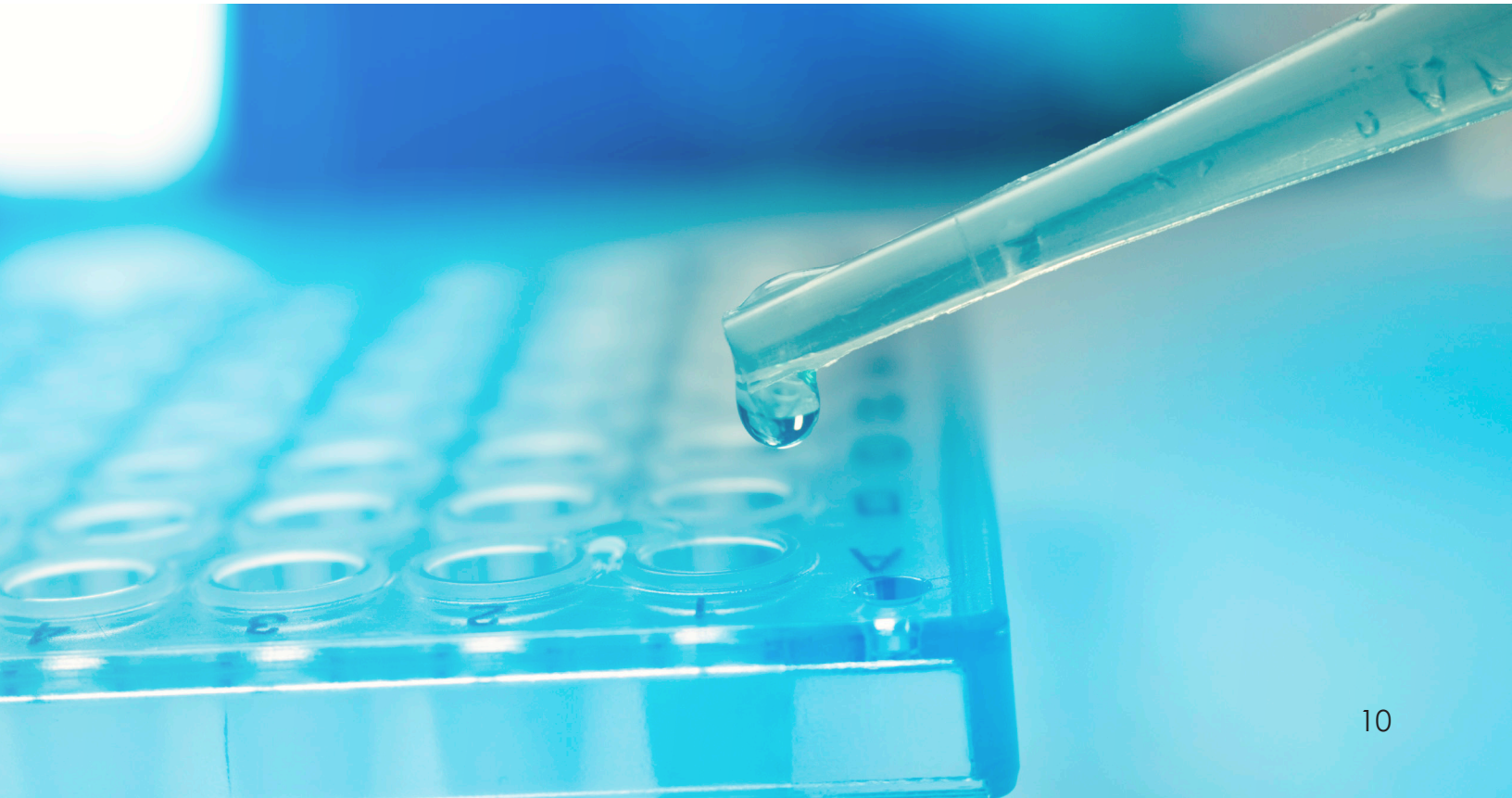
Bioanalytical

We offer a comprehensive portfolio of bioanalytical services for customized GLP-compliant Bioanalytical MS/MS method development, validation and sample analysis. We are focused on providing highly sensitive assays over a large detection range to ensure the success of your complex drug discovery and development program. Our highly skilled staff of experienced scientists is supported by three different **LC/MS platforms**:

- SCIEX 6600
- SCIEX 4000
- Thermo TSQ Quantum Ultra

We deliver rapid and reproducible bioanalytical data of the highest quality to facilitate decisions concerning your drug candidate.

- Method development for compounds including peptides, amino acids, macrolides, and routine small molecules
- High throughput sample analysis with rapid turnaround
- Method validation following Crystal City and Organisation for Economic Cooperation and Development (OECD) guidelines
- Development of sensitive, reproducible assays for ocular and other target tissues
- Multiple extraction techniques:
    - Solid Phase Extraction (SPE)
    - Supported Liquid Extraction (SLE)
    - Protein Precipitation (PPT)



Ligand Binding & Other Assays

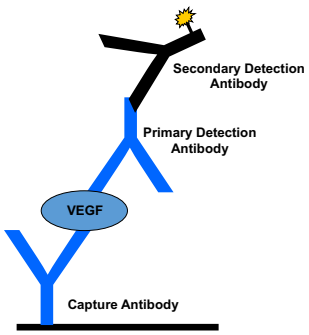
PharmOptima is experienced in the development, validation, and operation of ligand binding assays which provide critical data to support the safety and effectiveness of drugs and biologic products. Assays can be optimized to extend analytical range or add additional matrices. We pay particular attention to assay details which are crucial for successful and reproducible results to support your development program.

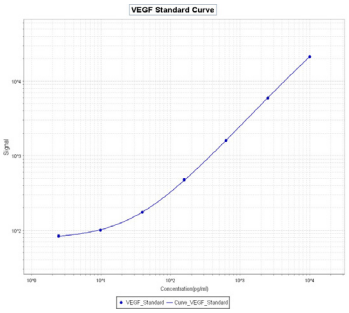
- **Immunoassay Development Platforms**
  - o Traditional colorimetric ELISA (HRP, AP)
  - o MesoScale Discovery electrochemiluminescence (ECL) multiplex immunoassays

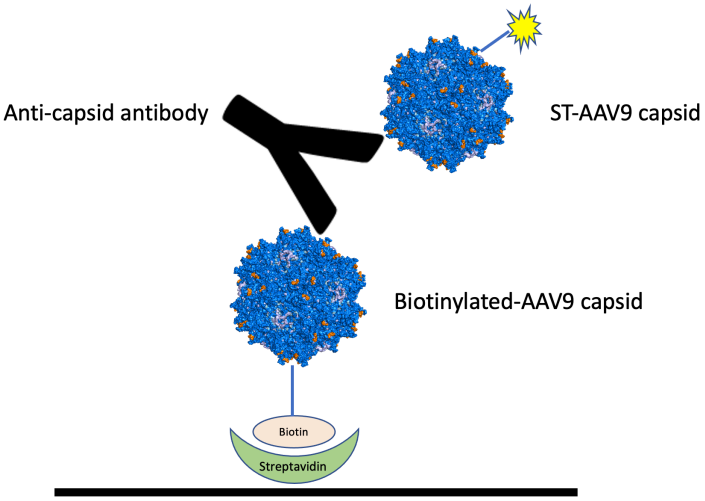
Our qualified biomarker assays include:

- Industry recognized proprietary SMN assay in whole blood
- Ocular disease
- Spinal muscular atrophy
- Nonalcoholic steatophatitis (NASH)
- Oncology
- Neurological Disease
- STING
- Adeno-associated viruses

Sandwich Ligand binding assay







Molecular Biology and Biochemistry

PharmOptima offers services in molecular biology, protein expression, protein purification, as well as structural and physicochemical characterization. Through our expertise we can optimize your antigens to improve the efficiency and reproducibility of your immunoassay.

- Protein Expression in Eukaryotic cells
  - o Mammalian cell
  - o Insect cell/Baculovirus
- Protein Purification and Characterization
  - o Affinity chromatography (His-tag, Protein-A/G, Antibody)
- Antibody Purification and Labeling
  - o HRP
  - o Sulfo-tag Ruthenium for ECL applications
- Stable clonal mammalian cell line generation and characterization

Premiere Biomarker Development

We have the expertise and experience to clone and express proteins for novel biomarker assay development if what you need is not commercially available. Utilizing MSD Technology*, biomarkers are available from human, rat, mouse and non-human primate in many cases.

- metabolic markers
- oncology markers
- vascular markers
- cytokines and chemokines
- cell signaling pathways
- Alzheimer's (Aβ38, Aβ40, Aβ42 and Tau, Total Tau)
- kidney injury
- cardiac and muscle
- liver injury
- inflammation

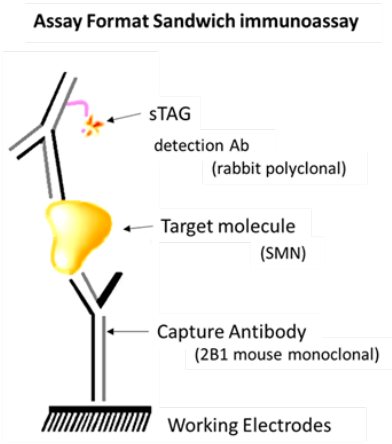
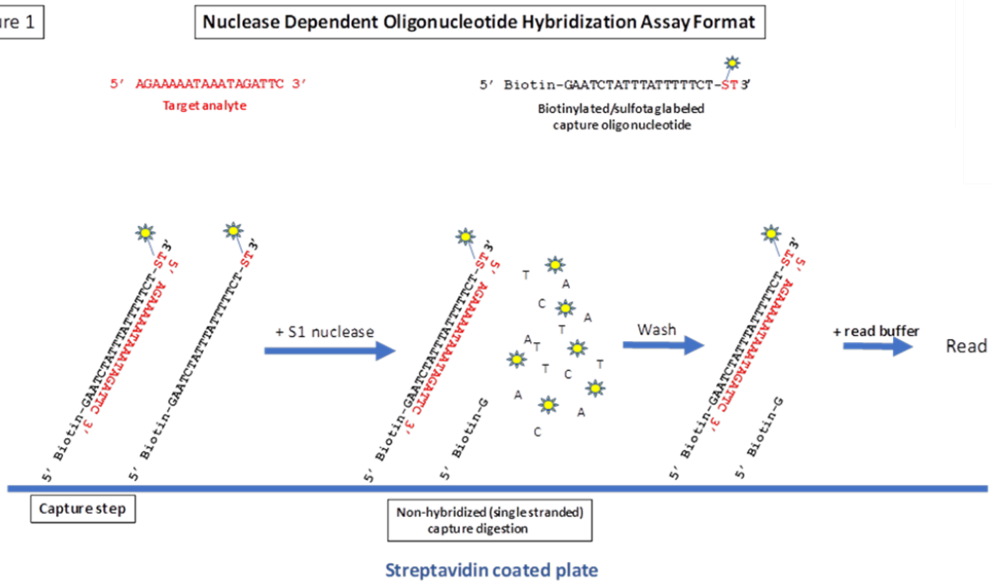


Figure 1



In Vivo Techniques

PharmOptima is a leading provider of services in developing, characterizing, and maintaining genetically modified and disease-induced models. Our team of highly skilled personnel, will lead your *in vivo* studies to thoroughly assess the safety and efficacy of your molecules.

We have the expertise to conduct preclinical studies in dosing administration for multiple species with multiple routes of administration.

Species:

- Rodent
- Rabbit
- Guinea pig

Routes of Administration:

- Subcutaneous (SQ)
- Oral (PO)
- Intravenous (IV)
- Intramuscular (IM)
- Speciated Ocular Dosing
- Topical

Our team of highly skilled personnel has extensive experience and **surgical expertise** necessary to expedite your preclinical program:

- Full tissue necropsy
- CSF collection in rodents
- Full pathology services
- Micro dissection of ocular tissues
- Tissue distribution
- Infusion studies – short and long term
- Whole body perfusion
- Behavioral studies – FOB, gate-analysis, visual acuity
- Transgenic colony breeding and maintenance
- Colony isolation via hepafilter biobubble

Madeline Farley, Ph.D., Managing Director

Dr. Farley is the Managing Director of PharmOptima in Portage, Michigan. Dr. Farley has 15 years of experience in neuroscience research and preclinical contract work, emphasizing molecular biology, biochemistry, biophysics and disease modeling. Dr. Farley joined PharmOptima in 2021 as a Senior Scientist within the Biochemistry group. Apart from her role in Biochemistry, she has worked closely with the Vivarium to establish ocular disease models within the Ocular Center of Excellence. Before joining PharmOptima, Dr. Farley investigated injury signaling pathways underlying neurodegenerative disease and neuronal injury using transgenic mice and AAV-based gene delivery systems targeting neurons within the retina. Dr. Farley received her BS in Biochemistry, with a minor in Mathematics, from Centenary College of Louisiana. She earned her Ph.D. in Cellular and Molecular Neuroscience at The University of Texas Health Science Center in Houston, TX. She completed postdoctoral fellowships at both McGovern Medical School at UTHealth and Baylor College of Medicine. Dr. Farley has been a recipient of a vision sciences postdoctoral fellowship through the National Eye Institute and an individual NRSA predoctoral fellowship through the National Institute of Neurological Disorders and Stroke.

Phillip G. Zaworski, Biochemistry Team Lead/Senior Scientist

Phillip is a Sr. Research Scientist with over 35 years of experience in drug discovery research. His specialties include mammalian cell line development, clonal isolation, multiplex immunoassay development using Meso Scale Discovery platform, insect cell and mammalian cell expression, and cell based assay development. He oversees work flow management, client consultation, contract development and applies innovative methodologies to solve production issues. He received a BS in Botany/Zoology and MS in Microbiology from the University of Idaho in Moscow, Idaho. Phillip has co-authored 13 peer reviewed publications. In his spare time Phillip enjoys a hobby farm with horses, cattle, chickens, dogs, cats and hay.

Daniel Skutnik, Facility Manager/Study Director

Dan is the facility manager of PharmOptima and study director for Pharmacokinetics. With 15 years of experience, he leads departmental initiatives to enhance and advance business development and pharmacokinetic services, including ocular pharmacokinetics. He is responsible for the overall planning and conduct of nonclinical, non-GLP studies (from dose-ranging studies to long-term exposure and safety), data interpretation, and reporting, as well as partnering with sponsors to further expand their discovery and development efforts. Dan received a BS in Biomedical Sciences from Western Michigan University in Kalamazoo, Michigan. Mr. Skutnik has co-authored several abstracts and posters in the field of ocular pharmacokinetics and toxicology.

David Bailey, Team Leader/Senior Research Scientist

David is a Senior Research Scientist with over 30 years of experience in drug discovery research. His specialties include LC-MS/MS method development, validation and sample analysis in a GLP regulated bioanalytical lab environment, high throughput bioanalytical sample analysis for discovery stage pharmaceuticals, and biomarkers in various matrices. He received a BS in Natural Sciences and Environmental Sciences from Purdue University in West Lafayette, Indiana and a MBA from Western Michigan University in Kalamazoo, Michigan.

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